

L1 2' GLUTAMATE (W) TRANSPORTER

1. 5,424,185, Jun. 13, 1995, Human high-affinity neurotransmitter uptake system; Dominic M. Lam, et al., 435/6, 29, 172.3, 240.1, 240.2; 436/92, 501, 815, 816; 530/350; 536/23.1; 935/6, 9, 78 [IMAGE AVAILABLE]

US PAT NO: 5,424,185 [IMAGE AVAILABLE]

L1: 1 of 2

ABSTRACT:

Non-primate or primate cells are provided comprising a functional human transporter for neurotransmitter uptake. The cells allow for dissection of the mechanism of neurotransmitter transport, as well as screening for agonists and antagonists of the neurotransmitter with respect to its uptake. Methods are provided for producing such cells. Specifically, the cells are transformed with human DNA comprising the gene encoding for the neurotransmitter transporter, whereby this protein(s) is expressed and incorporated into the plasma membrane and is capable of functioning to transfer the neurotransmitter from the extracellular space to intracellular domains. The physiological, kinetic and pharmacological characteristics of transport in these cells conform to known characteristics of high-affinity neurotransmitter transport in the CNS.

2. 5,403,861, Apr. 4, 1995, Substituted guanidines and derivatives thereof as modulators of neurotransmitter release and novel methodology for identifying neurotransmitter release blockers; Stanley M. Goldin, et al., 514/634, 150, 506, 519, 588, 616, 623 [IMAGE AVAILABLE]

US PAT NO: 5,403,861 [IMAGE AVAILABLE]

L1: 2 of 2

ABSTRACT:

Modulators of neurotransmitter release including substituted guanidines, N"-aminoguanidines, and N,N'N",N"'-tetrasubstituted hydrazinedicarboximidamides, and pharmaceutical compositions thereof are disclosed. Also disclosed are methods involving the use of such neurotransmitter release modulators for the treatment or prevention of pathophysiologic conditions characterized by the release of excessive or inappropriate levels of neurotransmitters. Also disclosed are screening assays for compounds which selectively inhibit glutamate release. Also disclosed are methods of blocking voltage sensitive sodium and calcium channels in mammalian nerve cells.

L2 0 EXITATORY (W) AMINO (W) ACID (W) TRANSPORTER

L3 0 EAAT2

L4 0 EAAC1

L5 3 GLUTAMATE (5A) TRANSPORTER

L6 1 L5 NOT L1

1. 5,389,359, Feb. 14, 1995, Pharmaceutical preparation containing L-aspartate or L-asparagine for preventing ethanol toxicity, and process for preparation thereof; Sang C. Park, 514/561; 424/406; 426/75, 590, 592, 599; 514/557, 563, 578, 724, 811, 974 [IMAGE AVAILABLE]

US PAT NO: 5,389,359 [IMAGE AVAILABLE]

L6: 1 of 1

ABSTRACT:

Compositions containing L-aspartate or L-asparagine for use as additives to foods, soft drinks, vitamins, and the like are described. A method for preventing ethanol toxicity in a human subject is also provided.

GAT2 Swinmot

RESULT 1

ID GLT1 RAT STANDARD; PRT; 573 AA.

AC P31596;

DT 01-JUL-1993 (REL. 26, CREATED)

DT 01-OCT-1993 (REL. 27, LAST SEQUENCE UPDATE)

DT 01-OCT-1993 (REL. 27, LAST ANNOTATION UPDATE)

DE BRAIN SODIUM-DEPENDENT GLUTAMATE/ASPARTATE TRANSPORTER.

GN GLT-1.

OS RATTUS NORVEGICUS (RAT).

OC EUKARYOTA; METAZOA; CHORDATA; VERTEBRATA; TETRAPODA; MAMMALIA;

OC EUTHERIA; RODENTIA.

RN [1]

RP SEQUENCE FROM N.A.

RC TISSUE=BRAIN;

RM 93078876

RA PINES G., DANBOLT N.C., BJORAS M., ZHANG Y., BENDAHAN A., EIDE L.,

RA KOEPESELL H., STORM-MATHISEN J., SEEBERG E., KANNER B.I.;

RL NATURE 360:464-467 (1992).

RN [2]

RP REVISIONS TO 260-289.

RM 93292659

RA KANNER B.I.;

RL FEBS LETT. 325:95-99 (1993).

CC -!- FUNCTION: TRANSPORTS L-GLUTAMATE AND ALSO L- AND D-ASPARTATE.

CC ESSENTIAL FOR TERMINATING THE POSTSYNAPTIC ACTION OF GLUTAMATE BY

CC RAPIDLY REMOVING RELEASED GLUTAMATE FROM THE SYNAPTIC CLEFT. ACTS

CC AS A SYMPORT BY CO-TRANSPORTING SODIUM.

CC -!- PTM: GLYCOSYLATED.

CC -!- SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN.

CC -!- TISSUE SPECIFICITY: LOCALIZED IN BRAIN AND IS HIGHLY ENRICHED IN

CC THE PURKINJE CELL LAYER IN CEREBELLUM.

CC -!- SIMILARITY: BELONGS TO THE SODIUM:DICARBOXYLATE SYMPORTER FAMILY

CC (SDF).

DR EMBL; X67857; RNGLT.

DR PROSITE; PS00713; NA_DICARBOXYL_SYMP_1.

DR PROSITE; PS00714; NA_DICARBOXYL_SYMP_2.

KW TRANSPORT; TRANSMEMBRANE; GLYCOPROTEIN; SYMPORT.

FT	DOMAIN	1	44	CYTOPLASMIC (POTENTIAL).
FT	TRANSMEM	45	64	POTENTIAL.
FT	TRANSMEM	88	108	POTENTIAL.
FT	TRANSMEM	121	142	POTENTIAL.
FT	DOMAIN	143	238	EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM	239	258	POTENTIAL.
FT	TRANSMEM	279	300	POTENTIAL.
FT	TRANSMEM	316	338	POTENTIAL.
FT	TRANSMEM	405	429	POTENTIAL.
FT	TRANSMEM	436	458	POTENTIAL.
FT	CARBOHYD	205	205	POTENTIAL.

```
DB 3; Score 3933; Match 94.6%; QryMatch 96.3%; Pred. No.
0.00e+00;
Matches 543; Conservative 23; Mismatches 7; Indels 1;
Gaps 1;
```

Q MASTEGANNMPKQVEVRMPD^YSHLGSEEPK^YKHRHLGLRLCDKLGKNLLLT^YLT^YTVFGVILGAVC 60

Q y 6 1
GGLRLASPIHPDVVMLIAFFPGDILMRMLKMLILGLIISSLITGLSGLDAKASGRLGTRA 120

Q y 1 2 1
MVYYMSTTTIIAAVLGVILVLAIHGPNPKLKKQLGPGKKNDEVSSSLDAFLDLIRNLFPENL 180

Q y 1 8 1
VOACFOQIQTVTKKVLVAPPPDEEANATSAEVSLNETVTEVPEETKMVIKKGLEFKDGM 240

Q y 2 4 1
NVI¹GLIGFFIAFGTAMGKMGDOAKLMVDFENILNEIVMKLVIMIMWYSPLGIACLICGKI 300

Q y 3 0 1
IAIKDLEVVARQLGMYMVTVIIGLIITHGGTFLPLIYFVTVTRKNPFSLFAGIFOAWITALG 360

D b 3 6 0
tassagtlpvtfrclcdnlgidkrvtrfvlpgatinmdgtalyeavaaifiaqmngvil 419
|||||:|||||||

EAAT2
DNA

RESULT 1
LOCUS HSU03505 1800 bp mRNA PRI
13-OCT-1994
DEFINITION Human excitatory amino acid transporter2 mRNA,
complete cds.
ACCESSION U03505
KEYWORDS .
SOURCE human.
ORGANISM Homo sapiens
Eucaryotae; Metazoa; Chordata; Vertebrata;
Gnathostomata; Mammalia;
Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 1800)
AUTHORS Arriza, J.L., Fairman, W.A., Wendy, A., Wadiche, J.I.,
Murdoch, G.H.,
Kavanaugh, M.P. and Amara, S.G.
TITLE Functional comparisons of three glutamate transporter
subtypes
cloned from human motor cortex
JOURNAL J. Neurosci. 14, 5559-5569 (1994)
MEDLINE 94365697
REFERENCE 2 (bases 1 to 1800)
AUTHORS Arriza, J.L.
TITLE Direct Submission
JOURNAL Submitted (16-NOV-1993) Jeffrey L. Arriza, The Vollum
Institute,
Oregon Health Sciences University, 3181 SW Sam
Jackson Park Road,
Portland, OR 97201, USA
COMMENT NCBI gi: 487340
FEATURES Location/Qualifiers
source 1..1800
/organism="Homo sapiens"
/tissue_type="brain: motor cortex"
5'UTR 1..33
CDS 34..1758
/note="NCBI gi: 487341"
/codon_start=1
/product="excitatory amino acid
transporter2"
/translation="MASTEGANNMPKQVEVRMPDSHLGSEEPKHRHLGLRLCDKLGKN
LLLTLTVFGVILGAVCGLLRLASPIHPDVVMLIAFPGDILMRMLKMLILPLIISSLI
TGLSGLDAKASGRLGTRAMVYYMSTTIIAAVLGVILVLAIHGPNPKLKKQLGPGKKND
EVSSLD AFLDLIRNLFPENLVQACFQQIQTVTKKVLVAPPPDEEANATSAEVSLNET
VTEVPEETKMVIKKGLEFKDGMNVLGLIGFFIAFGIAMGKMGDQAKLMVDFFNILNEI
VMKLVIMIMWYSPLGIACLICGKIIAIKDLEVVARQLGMYMVTVIIGLIIHGGIFLPL
IYFVVTRKNPFSLFAGIFQAWITALGTASSAGTLPVTFRCLEENLGIDKRVTRFVLPV

Q851. J65 ✓

GATINMDGTALYEAVAAIFIAQMNGVVLDDGGQIVTVSLTATLASVGAASIPSAGLVTM
LLILTAVGLPTEDISLLVAVDWLLDRMRTSVNVVGDSFGAGIVYHLSKSELDTIDSQH
RVHEDIEMTKTQSIYDDMKNHRESNSNQCVYAAHNSVIVDECKVTLAANGKSADCSVE
EEPWKREK"

3'UTR 1759..1800
BASE COUNT 439 a 425 c 486 g 450 t
ORIGIN

DB 112; Score 1794; Match 99.8%; QryMatch 99.7%; Pred.
No. 0.00e+00;
Matches 1797; Conservative 0; Mismatches 3; Indels
0; Gaps 0;

Db 1
gatagtgtgaagaggagggcggtcccagaccatggcatctacggaaggtgccacaat 60

|||||
Qy 1
GATAGTGCTGAAGAGGAGGGGCGTTCCCAGACCATGGCATCTACGGAAGGTGCCAACAAT 60

Db 61
atgcccagcaggtggaagtgcgaatgccagacagtcacatcttggtcagaggaaccaag 120

|||||
Qy 61
ATGCCCAAGCAGGTGGAAGTGCGAATGCCAGACAGTCATCTTGGCTCAGAGGAACCCAAG 120

Db 121
caccggcacctgggcctgcgccctgtgtgacaagctggggaagaatctgctgctcacctg 180

|||||
Qy 121
CACCGGCACCTGGGCCTGCGCCTGTGTGACAAGCTGGGGAAGAATCTGCTGCTCACCTG 180

Db 181
acggtgtttggtgtcatcctgggagcagtggtgtggagggtctcttcgcttggtcatctccc 240

|||||
Qy 181
ACGGTGTTTGGTGTCATCCTGGGAGCAGTGTGTGGAGGGCTTCTTCGCTTGGCATCTCCC 240

Db 241
atccaccctgatgtggttatgttaatagccttcccaggggatatactcatgaggatgcta 300

|||||
Qy 241
ATCCACCCTGATGTGGTTATGTTAATAGCCTTCCCAGGGGATATACTCATGAGGATGCTA 300

Db 301
aaaatgctcattctccctctaatacatctccagcttaatacacagggttggtcaggcctggat 360

|||||

RESULT 2
 LOCUS HSU01824 1969 bp mRNA PRI
 10-JUN-1994
 DEFINITION Human glutamate/aspartate transporter II mRNA,
 complete cds.
 ACCESSION U01824
 KEYWORDS .
 SOURCE human.
 ORGANISM Homo sapiens
 Eucaryotae; Metazoa; Chordata; Vertebrata;
 Gnathostomata; Mammalia;
 Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (sites)
 AUTHORS Shashidharan, P., Wittenberg, I. and Plaitakis, A.
 TITLE Molecular cloning of human brain glutamate/aspartate
 transporter II
 JOURNAL Biochim. Biophys. Acta 1191, 393-396 (1994)
 MEDLINE 94227088
 REFERENCE 2 (bases 1 to 1969)
 AUTHORS Shashidharan, P.
 TITLE Direct Submission
 JOURNAL Submitted (14-SEP-1993) Pullanipally Shashidharan,
 Mount Sinai School of Medicine, Neurology, One Gustave L Levy
 Place, New York,
 New York 10029, USA
 COMMENT NCBI gi: 498250
 FEATURES Location/Qualifiers
 source 1..1969
 /clone="HBGT2"
 /clone_lib="cDNA library"
 /organism="Homo sapiens"
 /tissue type="brain stem"
 CDS 179..1876
 /note="NCBI gi: 498251"
 /codon_start=1
 /product="glutamate/aspartate transporter
 II"

/translation="MPKQVEVRMHDSHLGSEEPKHRHLGLRLCDKLGKNLLLTQVFG
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 DLIRNLFPENLVQACFQQIQTVTKKVLVAPPPDEEANATSAVVSLNETVTEVPEETK
 MVIKKGLEFKDGMNVLGLIGFFIAFGIAMGKMGDQAKLMVDFFNILNEIVMKLVIMIM
 WYSPLGIACLICGKIIAIKDLEVVARQLGMYMVTVIIIGLIIHGGIFLPLIYFVVTRKN
 PFSFFAGIFQAWITALGTASSAGTLPVTFRCLEENLGIDKRVTRFVLPVGATINMDGT
 ALYEAVAAIFIAQMNGVVLDGGQIVTVSLTATLASVGAASIPSAGLVTMLLILTAVGL

PTEDISLLVAVDWLLDRMRTSVNVVGDSFGAGIVYHLSKSELDTIDSQHRVHEDIEMT

KTQSIYDDMKNHRESNSNQCVYAAHNSVIVDECKVTLAANGKSADCSVEEEPWKREK"

BASE COUNT 485 a 466 c 526 g 492 t

ORIGIN

DB 111; Score 1724; Match 99.1%; QryMatch 95.8%; Pred.
No. 0.00e+00;
Matches 1740; Conservative 0; Mismatches 16; Indels
0; Gaps 0;

Db 163
ggacagtgcccaacaatatgcccaagcaggtggaagtgcgaatgcacgacagtcattcttg 222

|||||

|||||

Qy 45
GGAAGGTGCCAACAAATATGCCCAAGCAGGTGGAAGTGCGAATGCCAGACAGTCATCTTGG 104

Db 223
ctcagaggaacccaagcaccggcacctgggcctgcgcctgtgtgacaagctggggaagaa 282

|||||

Qy 105
CTCAGAGGAACCCAAGCACCGGCACCTGGGCCTGCGCCTGTGTGACAAGCTGGGGAAGAA 164

Db 283
tctgctgctcaccctgcaggtgtttggtgtcatcctgggatcagtggtgtggagggcttct 342

|||||

|||||

Qy 165
TCTGCTGCTCACCTGACGGTGTTTGGTGTCATCCTGGGAGCAGTGTGTGGAGGGCTTCT 224

Db 343
tcgcttggcatctcccatccaccctgatgtggttatgttaatagccttcccaggggatat 402

|||||

Qy 225
TCGCTTGGCATCTCCCATCCACCCTGATGTGGTTATGTTAATAGCCTTCCCAGGGGATAT 284

Db 403
actcatgaggatgctaaaaatgctcattctccctctaatacatctccagcttaatacacagg 462

|||||

|||||

Qy 285
ACTCATGAGGATGCTAAAAATGCTCATTCTGGGTCTAATCATCTCCAGCTTAATCACAGG 344

Db 463
gttgtcaggcctggatgctaaggctagtggccgcttgggcacgagagccatggtgtatta 522

|||||

Qy 345
GTTGTCAGGCCTGGATGCTAAGGCTAGTGGCCGCTTGGGCACGAGAGCCATGGTGTATTA 404

RESULT 3
 LOCUS HSGLUTTR 1912 bp RNA PRI
 08-NOV-1994
 DEFINITION H.sapiens mRNA for glutamate transporter.
 ACCESSION Z32517
 KEYWORDS glutamate transporter.
 SOURCE human.
 ORGANISM Homo sapiens
 Eukaryotae; mitochondrial eukaryotes;
 Metazoa/Eumycota group;
 Metazoa; Eumetazoa; Bilateria; Coelomata;
 Deuterostomia; Chordata;
 Vertebrata; Gnathostomata; Osteichthyes;
 Sarcopterygii; Choanata;
 Tetrapoda; Amniota; Mammalia; Theria; Eutheria;
 Archonta; Primates;
 Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 1912)
 AUTHORS Manfras,B.J., Rudert,W.A., Trucco,M. and Boehm,B.O.
 TITLE Cloning and characterization of a glutamate
 transporter cDNA from
 human brain and pancreas
 JOURNAL Biochim. Biophys. Acta 1195 (1), 185-188 (1994)
 MEDLINE 95002073
 REFERENCE 2 (bases 1 to 1912)
 AUTHORS Manfras,B.J.
 TITLE Direct Submission
 JOURNAL Submitted (07-APR-1994) to the EMBL/GenBank/DBJ
 databases. Manfras
 B. J., University of Ulm, Department of Internal
 Medicine,
 Robert-Koch-Str.8, Ulm, Germany, 89081
 COMMENT NCBI gi: 471246
 FEATURES Location/Qualifiers
 source 1..1912
 /organism="Homo sapiens"
 /clone="GLTRpal"
 /tissue_type="pancreas"
 /germline
 mRNA 1..1912
 CDS 90..1814
 /note="NCBI gi: 488752"
 /codon_start=1
 /product="glutamate transporter"

/translation="MASTEGANNMPKQVEVRMHDSHLGSEGPKHRHLGLRLCDKLGKN
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 EVSSLDAFLDLIRNLFPENLVQACFQQIQTVTKKVLVAPPPDEEANATSAVVSLLNET
 VTEVPEETKMVIKKGLEFKDGMNVLGLIGFFIAFAIPMGKMGDQGQADGGFLQHFERD

RESULT 5
 LOCUS RNGLT 1898 bp RNA ROD
 30-JUN-1993
 DEFINITION R.norvegicus mRNA for glutamate transporter.
 ACCESSION X67857 S49853
 KEYWORDS glt gene; transmembrane glycoprotein.
 SOURCE Norway rat.
 ORGANISM Rattus norvegicus
 Eukaryotae; mitochondrial eukaryotes;
 Metazoa/Eumycota group;
 Metazoa; Eumetazoa; Bilateria; Coelomata;
 Deuterostomia; Chordata;
 Vertebrata; Gnathostomata; Osteichthyes;
 Sarcopterygii; Choanata;
 Tetrapoda; Amniota; Mammalia; Theria; Eutheria;
 Glires; Rodentia;
 Sciurognathi; Myomorpha; Muridae; Murinae; Rattus.
 REFERENCE 1 (bases 1 to 1898)
 AUTHORS Kanner, B.
 TITLE Direct Submission
 JOURNAL Submitted (27-JUL-1992) to the EMBL/GenBank/DBJ
 databases. B.
 Kanner, The Hebrew University, Hadassah Medical
 School, P.O. Box
 1172, Jerusalem 91010, ISRAEL
 REFERENCE 2 (bases 1 to 1898)
 AUTHORS Pines, G., Danbolt, N.C., Bjoras, M., Zhang, Y.,
 Bendahan, A., Eide, L.,
 Koepsell, H., Storm-Mathisen, J., Seeborg, E. and
 Kanner, B.I.
 TITLE Cloning and expression of a rat brain L-glutamate
 transporter
 [published erratum appears in Nature 1992 Dec
 24-31; 360(6406):768]
 [see comments]
 JOURNAL Nature 360 (6403), 464-467 (1992)
 MEDLINE 93078876
 COMMENT NCBI gi: 56262
 FEATURES Location/Qualifiers
 source 1..1898
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 /tissue_type="brain"
 /cell_type="glial"
 /cell_line="rat brain"
 /clone_lib="lambda zap"
 CDS 99..1820
 /gene="GLT-1"
 /note="NCBI gi: 56263"
 /codon_start=1
 /product="Glutamate transporter"

/translation="MASTEGANNMPKQVEVRMHDSHLSSEEPKHRNLGMRMCDKLGKN
 LLLSLTVFGVILGAVCGLLRLAAPIHPDVVMLIAFPDILMRMLKMLILPLIISSLI

Lab
 ✓
 Q1. N2
 ufilm

RESULT 6
 LOCUS MMU11763 1960 bp mRNA ROD
 02-JAN-1995
 DEFINITION Mus musculus C57BL excitatory amino acid transporter
 2 mRNA,
 complete cds.
 ACCESSION U11763
 KEYWORDS .
 SOURCE mouse.
 ORGANISM Mus musculus
 Eukaryotae; Hyperchondria; Eukaryote crown group;
 Metazoa/Eumycota
 group; Metazoa; Eumetazoa; Bilateria; Coelomata;
 Deuterostomia;
 Chordata; Vertebrata; Gnathostomata; Osteichthyes;
 Sarcopterygii;
 Choanata; Tetrapoda; Amniota; Mammalia; Theria;
 Eutheria; Glires;
 Rodentia; Sciurognathi; Myomorpha; Muridae; Mus.
 REFERENCE 1 (bases 1 to 1960)
 AUTHORS Kirschner, M.A., Copeland, N.G., Gilbert, D.J.,
 Jenkins, N.A. and
 Amara, S.G.
 TITLE Mouse excitatory amino acid transporter EAAT2
 isolation,
 characterization, and proximity to neuroexcitability
 loci on mouse
 chromosome 2
 JOURNAL Unpublished
 REFERENCE 2 (bases 1 to 1960)
 AUTHORS Kirschner, M.A.
 TITLE Direct Submission
 JOURNAL Submitted (01-JUL-1994) Marc A. Kirschner, Vollum
 Institute/Neurology, Oregon Health Sciences
 University, 3181 Sam
 Jackson Park Rd., Portland, OR 97201, USA
 COMMENT NCBI gi: 607865
 FEATURES Location/Qualifiers
 source 1..1960
 /clone="pBSKmEAAT2"
 /clone_lib="lambdaZAPMB"
 /chromosome="2"
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 /strain="C57BL"
 /organism="Mus musculus"
 /tissue_type="brain"
 /dev_stage="adult"
 CDS 188..1906
 /note="EAAT2; NCBI gi: 607866"
 /codon_start=1
 /product="excitatory amino acid transporter
 2"

/translation="MASTEGANNMPKQVEVRMHDSHLSSDEPKHRNLGMRMCDKLGKN

LLLSLTVFGVILGAVCGLLRLASPIHPDVVMLIAFPGDILMRMLKMLILPLIISSLI
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EVSSLDAFLDLIRNLFPENLVQACFQQIQTVTKKVLVAPPSEEANTTKAVISMLNETM
NEAPEETKIVIKKGLEFKDGMNVLGLIGFFIAFGIAMGKMGEQAKLMVEFFNILNEIV
MKLVIMIMWYSPLGIACLICGKIIAIKDLEVVARQLGMYMITVIVGLIIHGGIFLPLI
YFVVTRKNPFSFFAGIFQAWITALGTASSAGTLPVTFRCLEDNLGIDKRVTRFVLPVG
ATINMDGTALYEAVAAIFIAQMNGVILDGGQIVTVSLTATLASIGAASIPSAGLVTML
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PWKREK"

BASE COUNT 464 a 504 c 539 g 453 t
ORIGIN

DB 119; Score 1317; Match 87.8%; QryMatch 73.2%; Pred.
No. 0.00e+00;
Matches 1570; Conservative 0; Mismatches 211; Indels
7; Gaps 3;

Db 168
gaggaggggt-tccccagcccatggcatcaacagaggggtgccaacaatatgccaagcag 226
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||| ||| ||| ||| ||| ||| ||| |||
Qy 13
GAGGAGGGGCGTTCCCAGACCATGGCATCTACGGAAGGTGCCAACAATATGCCCAAGCAG 72

Db 227
gtagaagtgcgcatgcatgacagccacctcagctccgatgagccaaagcaccgaaacctg 286
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Qy 73
GTGGAAGTGCGAATGCCAGACAGTCATCTTGGCTCAGAGGAACCCAAGCACCGGCACCTG 132

Db 287
ggcatgcgcatgtgcgacaagctggggaaaaatctcctgctctcactgactgtgtttggt 346
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Qy 133
GGCCTGCGCCTGTGTGACAAGCTGGGGAAGAATCTGCTGCTCACCTGACGGTGT TTGGT 192

Db 347
gtcatcctgggagcagtggtgtggcgggctgcttcgcttgcatcgcccatccaccctgat 406
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Qy 193
GTCATCCTGGGAGCAGTGTGTGGAGGGCTTCTTCGCTTGGCATCTCCCATCCACCCTGAT 252

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RESULT      1
ENTRY       A55676      #type complete
TITLE       excitatory amino acid transporter EEAT2 - mouse
ORGANISM    #formal_name Mus musculus #common_name house mouse
DATE        03-Mar-1995 #sequence_revision 03-Mar-1995
#text change
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03-Mar-1995
ACCESSIONS      A55676
REFERENCE       A55676
#authors        Kirschner, M.A.; Copeland, N.G.; Gilbert, D.J.;
Jenkins,        N.A.; Amara, S.G.
#journal        Genomics (1994) 24:218-224
#title          Mouse excitatory amino acid transporter EAAT2:
isolation,      characterization, and proximity to
neuroexcitability loci
                 on mouse chromosome 2.
#accession      A55676
##status        preliminary
##molecule_type mRNA
##residues      1-572 ##label KIR
##cross-references GB:U11763

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GENETICS
#gene      EEAT2
SUMMARY    #length 572  #molecular-weight 62030  #checksum
5318
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```
DB 10; Score 3917; Match 94.4%; QryMatch 95.9%; Pred. No.
0.00e+00;
Matches 542; Conservative 24; Mismatches 6; Indels 2;
Gaps 2;
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Q MASTEGANNMPKQVEVRMPDShLGSEEPKHRHLGLRLCDKLGKNLLLLTLTVFGVILGAVC 60 y 1

D b 6 1
ggllrlaspihpdvmliafpgdilmrmlkmlilpliisslitglsfldakasgrlgtra 120
| | | | | | | | | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | |

Q y 6 1
GGLRLASPIHPDVVMLIAFFPGDILMRMLKMLILGLIISSLITGLSGLDKASGRLGTRA 120

[illegible]

Q y 1 2 1
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RESULT      2
ENTRY       S28901      #type complete
TITLE       glutamate transport protein - rat
ORGANISM    #formal_name Rattus norvegicus #common_name Norway
rat
DATE        25-Feb-1994 #sequence_revision 25-Feb-1994
#text_change
            25-Feb-1994
ACCESSIONS  S28901
REFERENCE   S28901
            #authors    Pines, G.; Danbolt, N.C.; Bjoras, M.; Zhang, Y.;
Bendahan,   A.; Eide, L.; Koepsell, H.; Storm-Mathisen, J.;
Seeberg,    E.; Kanner, B.I.
            #journal     Nature (1992) 360:464-467 ✓
            #title       Cloning and expression of a rat brain L-glutamate
                        transporter.
            #accession    S28901
            ##status      preliminary
            ##residues     1-573 ##label PIN
SUMMARY      #length 573 #molecular-weight 61674 #checksum
2812

```

```
DB 12; Score 3623; Match 89.6%; QryMatch 88.7%; Pred. No.
0.00e+00;
Matches 516; Conservative 29; Mismatches 26; Indels 5;
Gaps 5;
```


RESULT 5
 ENTRY JC2084 #type complete
 TITLE glutamate transporter - human
 ORGANISM #formal_name Homo sapiens #common_name man
 DATE 30-Sep-1993 #sequence_revision 20-Aug-1994
 #text_change
 09-Sep-1994
 ACCESSIONS JC2084
 REFERENCE JC2084
 #authors Kawakami, H.; Tanaka, K.; Nakayama, T.; Inoue, K.;
 Nakamura,
 S.
 #journal Biochem. Biophys. Res. Commun. (1994) 199:171-176
 #title Cloning and expression of a human glutamate
 transporter.
 #accession JC2084
 ##molecule_type mRNA
 ##residues 1-542 ##label KAW
 COMMENT This protein removes glutamate from the synaptic clefts
 and prevent the elevation of extracellular glutamate
 concentrations.
 COMMENT This protein plays an important role in the onset and
 progress of neurodegeneration.
 KEYWORDS brain; glycoprotein; transmembrane protein
 FEATURE
 48-68 #domain transmembrane #status predicted
 #label TM1\
 91-111 #domain transmembrane #status predicted
 #label TM2\
 123-145 #domain transmembrane #status predicted
 #label TM3\
 235-258 #domain transmembrane #status predicted
 #label TM4\
 284-304 #domain transmembrane #status predicted
 #label TM5\
 317-340 #domain transmembrane #status predicted
 #label TM6\
 35,206,216 #binding_site carbohydrate (Asn) (covalent)
 #status
 predicted
 SUMMARY #length 542 #molecular-weight 59572 #checksum
 983
 DB 9; Score 1834; Match 53.7%; QryMatch 44.9%; Pred. No.
 6.10e-230;
 Matches 269; Conservative 112; Mismatches 108; Indels 12;
 Gaps 11;

D b 4 5
 lfrnafvllltvtavivgtlrgftlrpyrmsyrev-kyfsfpqellmrmlqmlvlppliiss 103
 | : | :: ||| :||:|:: | || :| : ::|||:|||| ||||
 |||||

RESULT 7
ENTRY S28902 #type complete
TITLE Glutamate transporter - Rabbit
ORGANISM #formal_name Oryctolagus cuniculus #common_name
domestic

rabbit
DATE 22-Nov-1993 #sequence_revision 22-Nov-1993
#text_change

22-Nov-1993
ACCESSIONS S28902
REFERENCE S28902
#authors Kanai, Y.; Hediger, M.A.
#journal Nature (1992) 360:467-471
#title Primary structure and functional characterization
of a

high-affinity glutamate transporter.
#accession S28902
##status preliminary
##residues 1-524 ##label KAN
SUMMARY #length 524 #molecular-weight 56938 #checksum
3688

DB 12; Score 1783; Match 55.8%; QryMatch 43.6%; Pred. No.
9.21e-223;
Matches 258; Conservative 94; Mismatches 102; Indels 8;
Gaps 7;

D b 2 0
llls-tvvavvlgivigvlvreylnstldkfyafpgeilmrmlklvilplivssmitg 78
|||: || :|:| | | |:| | : :|||:|||||:|:|
||:|:|

Q y 4 5
LLLTLTVFGVILGAVCGLLRLASPIHPDVVMLIAFPGDILMRMLKMLILGLISSLITG 104

D b 7 9
vaaldsnvgkigiravlyyfcttiiaivilgivlvvsikpgvtqkvdeidrtgstpevst 138
::|:|:| ||:| ||:| | ||| :|:|:|:| || :
|||:

Q y 1 0 5
LSGLDAKASGRLGTRAMVYYMSTTIIAAVLGVILVLAIHPGNPKLKKQLGPGKKNDEVSS 164

D b 1 3 9
vdamldlirnmfpenlvqacfqqykt-tree-vtasddtgkngteesvtavmttavsenr 196
:| | |||||:||||| | |:| |::| |:| |: :
:|:|

Q y 1 6 5
LDAFLDLIRNLFPENLVQACFQQIQTVTKKVLVAPPPDEEANATSAEVS-LLNETVTEVP 223

D b 1 9 7
tkeyrvv--gl-ysdginvlglivfclvfglvigkmgkgqilvdffnalsdatmkivqi 253
|: || : ||:|||| | : ||: :|||: : :||| | :
||:| :

Q y 2 2 4
EETKMVIKKGLEFKDGMNVLGLIGFFIAFGIAMGKMGDQAKLMVDFFNILEIVMKLVIM 283

RESULT 8
 ENTRY . A54856 #type complete
 TITLE high affinity glutamate transporter - human
 ORGANISM #formal_name Homo sapiens #common_name man
 DATE 04-Nov-1994 #sequence_revision 04-Nov-1994
 #text_change 04-Nov-1994

ACCESSIONS A54856
 REFERENCE A54856
 #authors Kanai, Y.; Stelzner, M.; Nussberger, S.; Khawaja, S.; Hebert, S.C.; Smith, C.R.; Hediger, M.A.
 #journal J. Biol. Chem. (1994) 269:20599-20606
 #title The neuronal and epithelial human high affinity glutamate transporter. Insights into structure and mechanism of transport.

#accession A54856
 ##status preliminary
 ##molecule_type mRNA
 ##residues 1-524 ##label KAN
 ##cross-references GB:U06469
 KEYWORDS glycoprotein; transmembrane protein
 SUMMARY #length 524 #molecular-weight 57098 #checksum 291

DB 9; Score 1750; Match 55.4%; QryMatch 42.8%; Pred. No. 4.04e-218;
 Matches 256; Conservative 93; Mismatches 105; Indels 8; Gaps 7;

D	b	2	0
vlls-tvaavvlgittgvlvrehnsnstlekfyfafpgeilmrmlkliilpliissmitg 78			
: : : : : : : : :			
:			
Q	y	4	5
LLLTLTVFGVILGAVCGLLRLASPIHPDVVMLIAFPGDILMRMLKMLILGLISSLITG 104			
D	b	7	9
vaaldsnvsgkiglraavllyfcttliavilgivlvvsikpgvtqkvgeiartgstpevst 138			
:: : : : : : : : :			
:			
Q	y	1	5
LSGLDAKASGRLGTRAMVYYMSTTIIAAVLGVILVLAIHPGNPKLKKQLGPGKKNDEVSS 164			
D	b	1	9
vdamldlirnmfpenlvqacfqqykt--kreevnpasdpemmnt-ee-sftavmttaisk 194			
: : : :			
::			
Q	y	1	5
LDAFLDLIRNLFPENLVQACFQQIQTVTKKVLVAPPPDEEANATSAEVSLNETVTEVPE 224			
D	b	1	9